

## **WHAT IS CLAIMED IS:**

1. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising irradiating said biological material with radiation for a time effective to sterilize said biological material at a rate effective to sterilize said biological material and to protect said biological material from said radiation.

2. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising:

(i) adding to said biological material at least one stabilizer in an amount effective to protect said biological material from said radiation; and

(ii) irradiating said biological material with a suitable radiation at an effective rate for a time effective to sterilize said biological material.

3. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising:

(i) reducing the residual solvent content of said biological material to a level effective to protect said biological material from said radiation; and

(ii) irradiating said biological material with a suitable radiation at an effective rate for a time effective to sterilize said biological material.

4. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising:

(i) reducing the temperature of said biological material to a level effective to protect said biological material from said radiation; and

(ii) irradiating said biological material with a suitable radiation at an effective rate for a time effective to sterilize said biological material.

5. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising:

(i) applying to said biological material at least one stabilizing process selected from the group consisting of

(a) reducing the residual solvent content of said biological material,  
(b) reducing the temperature of said biological material, and  
(c) adding at least one stabilizer to said biological material; and  
(ii) irradiating said biological material with a suitable radiation at an effective rate for a time effective to sterilize said biological material, wherein said at least one stabilizing process and the rate of irradiation are together effective to protect said biological material from said radiation.

6. A method for sterilizing a biological material which contains a non-aqueous solvent and that is sensitive to radiation, said method comprising:

(i) applying to said biological material at least two stabilizing processes selected from the group consisting of

- (a) reducing the residual solvent content of said biological material,
- (b) reducing the temperature of said biological material, and
- (c) adding at least one stabilizer to said biological material; and

(ii) irradiating said biological material with a suitable radiation at an effective rate for a time effective to sterilize said biological material, wherein said at least two stabilizing processes are together effective to protect said biological material from said radiation and further wherein said at least two stabilizing processes may be performed in any order.

7. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said non-aqueous solvent is an organic solvent.

8. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 3.0 kGy/hour.

9. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 2.0 kGy/hr.

10. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 1.0 kGy/hr.

11. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said effective rate is not more than about 0.3 kGy/hr.

12. The method according to claim 2, 3, 4, 5 or 6, wherein said effective rate is more than about 3.0 kGy/hour.

13. The method according to claim 2, 3, 4, 5 or 6, wherein said effective rate is at least about 6.0 kGy/hour.

14. The method according to claim 2, 3, 4, 5 or 6, wherein said effective rate is at least about 18.0 kGy/hour.

15. The method according to claim 2, 3, 4, 5 or 6, wherein said effective rate is at least about 30.0 kGy/hour.

16. The method according to claim 2, 3, 4, 5 or 6, wherein said effective rate is at least about 45 kGy/hour.

17. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said biological material which contains a non-aqueous solvent is maintained in a low oxygen atmosphere.

18. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said biological material which contains a non-aqueous solvent is maintained in an atmosphere comprising at least one noble gas or nitrogen.

19. The method according to claim 18, wherein said noble gas is argon.

20. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said biological material which contains a non-aqueous solvent is maintained in a vacuum.

21. The method according to claim 3, 5 or 6, wherein said residual solvent content is reduced by a method selected from the group consisting of lyophilization, drying, concentration, addition of solute, evaporation, chemical extraction, spray-drying and vitrification.

22. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 15%.

23. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 10%.

24. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 3%.

25. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 2%.

26. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 1%.

27. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 0.5%.

28. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 0.08%.

29. The method according to claim 1, 2, 3, 4, 5 or 6, wherein at least one sensitizer is added to said biological material which contains a non-aqueous solvent prior to said step of irradiating said biological material.

30. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said biological material which contains a non-aqueous solvent contains at least one biological contaminant or pathogen selected from the group consisting of viruses, bacteria, yeasts, molds, fungi, parasites and prions or similar agents responsible, alone or in combination, for TSEs.

31. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is an antioxidant.

32. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a free radical scavenger.

33. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a combination stabilizer.

34. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a ligand.

35. The method according to claim 37, wherein said ligand is heparin.

36. The method according to claim 2, 5 or 6, wherein said at least one stabilizer reduces damage due to reactive oxygen species.

37. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine;  $\alpha$ -lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; n-propyl gallate, coumaric acid, and mixtures of two or more thereof.

38. The method according to claim 37, wherein said mixtures of two or more stabilizers are selected from the group consisting of: mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester

thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of uric acid, or a salt or ester thereof;  $\alpha$ -lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; n-propyl gallate, coumaric acid and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; and mixtures of ethanol and acetone.

39. The method according to claim 2, 5 or 6, wherein said at least one stabilizer is a dipeptide stabilizer.

40. The method according to claim 39, wherein said dipeptide stabilizer is selected from the group consisting of glycyl-glycine (Gly-Gly), carnosine and anserine.

41. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is corpuscular radiation or electromagnetic radiation, or a mixture thereof.

42. The method according to claim 41, wherein said electromagnetic radiation is selected from the group consisting of radio waves, microwaves, visible and invisible light, ultraviolet light, x-ray radiation, gamma radiation and combinations thereof.

43. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is gamma radiation.

44. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is E-beam radiation.

45. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is visible light.

46. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is ultraviolet light.

47. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is x-ray radiation.

48. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is polychromatic visible light.
49. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is infrared.
50. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said radiation is a combination of one or more wavelengths of visible and ultraviolet light.
51. The method according to claim 1, 2, 3, 5 or 6, wherein said irradiation is conducted at ambient temperature.
52. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted at a temperature below ambient temperature.
53. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted below the freezing point of said biological material which contains a non-aqueous solvent.
54. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said irradiation is conducted below the eutectic point of said biological material which contains a non-aqueous solvent.
55. The method according to claim 1, 2, 3, 5 or 6, wherein said irradiation is conducted at a temperature above ambient temperature.
56. A composition comprising at least one biological material which contains a non-aqueous solvent and at least one stabilizer in an amount effective to preserve said biological material for its intended use following sterilization with radiation.

57. A composition comprising at least one biological material which contains a non-aqueous solvent, wherein the residual solvent content of said biological material is at a level effective to preserve said biological material for its intended use following sterilization with radiation.

58. The composition of claim 57, wherein said residual solvent content is less than about 15%.

59. The composition of claim 57, wherein said residual solvent content is less than about 10%.

60. The composition of claim 57, wherein said residual solvent content is less than about 5%.

61. The composition of claim 57, wherein said residual solvent content is less than about 2%.

62. The composition of claim 57, wherein said residual solvent content is less than about 1%.

63. The composition of claim 57, wherein said residual solvent content is less than about 0.5%.

64. The composition of claim 57, wherein said residual solvent content is less than about 0.08%.

65. The composition of claim 56 or 57, wherein said biological material which contains a non-aqueous solvent is glassy or vitrified.

66. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 0.5%.

67. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 1%.

68. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 5%.

69. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 10%.

70. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 15%.

71. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 20%.

72. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 25%.

73. The composition of claim 56 or 57, wherein the total protein concentration of said biological material which contains a non-aqueous solvent is at least about 50%.

74. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said non-aqueous solvent is selected from the group consisting of glycerol, DMSO, ethanol, acetone and PPG.

75. The method according to claim 74, wherein said PPG is PPG 400, PPG 1200 or PPG 2000.

76. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 0%.

77. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 1%.

78. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 2.4%.

79. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 4.8%.

80. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 7%.

81. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 9%.

82. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 10%.

83. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 20%.

84. The method according to claim 3, 5 or 6, wherein said residual solvent content is about 33%.

85. The method according to claim 3, 5 or 6, wherein said residual solvent content is less than about 33%.

86. The composition of claim 56, wherein said at least one stabilizer is selected from the group consisting of: ascorbic acid or a salt or ester thereof; glutathione; 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; uric acid or a salt or ester thereof; methionine; histidine; N-acetyl cysteine;  $\alpha$ -lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; n-propyl gallate, coumaric acid, and mixtures of two or more thereof.

87. The composition of claim 86, wherein said mixtures of two or more stabilizers are selected from the group consisting of: mixtures of ascorbic acid, or a salt or ester thereof, and uric acid, or a salt or ester thereof; mixtures of ascorbic acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of ascorbic acid, or a salt or ester thereof, uric acid, or a salt or ester thereof, and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; mixtures of uric acid, or a salt or ester thereof;  $\alpha$ -lipoic acid; sodium formaldehyde sulfoxylate; gallic acid or a derivative thereof; n-propyl gallate, coumaric acid and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid; and mixtures of ethanol and acetone.

88. A method for prophylaxis or treatment of an infection or disease in a mammal comprising administering to a mammal in need thereof an effective amount of a biological material made according to a method of one of claims 1-6.

89. The method according to claim 1, 2, 3, 4, 5 or 6, wherein said biological material is selected from the group consisting of urokinase, immunoglobulin, thrombin, trypsin, albumin, purified protein factor and tissue.

90. The method according to claim 89, wherein said tissue is selected from the group consisting of heart valves and demineralized bone matrix.